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CDKL5 DEFICIENCY DISORDER (CDD): CASE STUDY OF A CDD WARRIOR

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ABSTRACT

Many cases of gene linked diseases are surfacing these days. CDKL5 Deficiency Disorder (CDD) is one of them. CDD is caused by mutations in the CDKL5 gene and has been increasingly recognized as a distinct clinical entity in the last decade. Initially, CDD has been described as an early seizure variant of Rett syndrome, CDKL5 disorder is now considered an independent entity. It is a genetic disorder that causes mild to severe seizures, developmental delays and severe cognitive disability. This case study is an attempt to understand CDD on a personal level by conducting an in-depth study of a child with CDD. This study is undertaken to understand various developmental aspects of a child with CDD, and further to explore their daily routine, specific problems and success of treatment given. This study is also an attempt to understand the parents' prospective of the child's ailment and their struggle to provide appropriate treatment to them.

KEYWORDS: CDKL5, CDD, Rett syndrome, CDD warrior.

INTRODUCTION:

Mutations in the CDKL5 gene causes a rare kind of disorder known as CDKL5 Deficiency Disorder (CDD), and has been increasingly recognized as a distinct clinical entity in the last decade. Initially CDD is described as an early seizure variant of Rett syndrome, CDKL5 disorder is now considered as an independent entity (Mangatt et.al, 2016). CDD is one of the most common monogenetic epileptic disorders, as incidence of CDD at approximately one in 40,000 live births shows its severity. Due to the fact that CDKL5 is located on the X chromosome, the prevalence of CDD among women is four times higher than in men (Jakimiec, Paprocka and Smigiel, 2020). It is a genetic disorder that causes mild to severe seizures, developmental delays and severe cognitive disability. Patients living with CDD show a significant neurodevelopmental delay, including severe hypotonia, motor and visual impairment, and little to no communication skills (Haenderson, 2020). Due to this, most CDD patients are always dependent on others for care for their entire life.

Some case studies and blog posts are available on children with CDKL5 deficiency disorder. Few of them are as follows:

(CDKL5 Spotlight on Isabella, 2019) Alexia, mother of Isabella, a CDD warrior girl, states that when Isabella was around one year old, they received her CDKL5 diagnosis. After deducing the cause for Isabella's seizures, things took a turn for the worse for the family. Currently, she is in physical therapy, occupational therapy and speech therapy. Weekly she attends each therapy 2-3 times, and other times Alexia is constantly doing activities with Isabella to stimulate her senses. Within the last year she has accomplished a lot.

(Spotlight on Skylar, 2021) Lauren, mother of Skylar, mentions that when Skylar was just two weeks old, she and her spouse observed some involuntary jerking movements in her feet. They started her early intervention at 5 months of age shortly after receiving the diagnosis. She was on track development until about 6 months of age as in-home physical and occupational therapies were given to her. However, due to the COVID-19 pandemic and following lockdown, all therapies were done online. Now, her deficits being more prominently observed.

(CDKL5 Spotlight on Toryn, 2020) Mylie, Toryn's mother, shares that Toryn's seizures began at the age of 8 months and she had them hourly. She was hospitalized and put on medications. Such severe seizures continued even after medication. Some medicines made her loose her sense of self; making it hard for her to function, smile, laugh and others even took her appetite. She says that one does not just fight the disorder, but also fights to find not only a medication that works, but one that doesn't suppress the child as well. In the last few months Toryn has made tremendous progress with gross and fine motor skills. After removing one medication, her personality is brightening up again.

(CDKL5 Spotlight on Olivia, 2020) Nicole, mother of Olivia, says that Olivia was just 8 weeks old when she had her first seizures. She further added that they didn't realize that was just the beginning of the real culprit and her lifelong fight with CDKL5. After a long list of diagnostic tests, it was confirmed. Olilvia was suffering from nocturnal seizures during which she can spit out or vomit. She shows signs of Cortical Vision Impairment (CVI), meaning her brain and eyes aren't able to coordinate and identify what she is seeing. When her body is working to perform actions like sitting, she tends to look down a lot as she has difficulty in seeing during these times. However, she loves to see light and responds positively to it. Her motor skills are still lacking as she's unable to sit, reach and grab object and bring them to her mouth. She is undergoing several therapies.

(CDKL5 Spotlight on Rian, 2020) Danielle, Rian's mother, shares that through the Special Intervention program, Rian started PT and Special Education. Apart from that, she's also undergoing Physical Therapy, Feeding/Speech Therapy, Occupational Therapy and Vision Therapy.

MATERIAL AND METHOD:

The given case study has been taken up to get first-hand knowledge regarding the developmental aspects of a child, Amaaya, suffering with CDD by directly interviewing the parents. A personal data sheet was prepared to collect the data regarding demographic and personal details of the case. A semi-structured interview schedule was prepared and utilized to collect data by interviewing the parents through an online meeting.

CASE HISTORY:

Name: Amaaya

Birth Year: 2017

Age: 4 Years

Father's detail: Age-38 years, Qualification- PG, Job.

Mother's detail: Age- 37 year, Qualification- PG, Job.

Mother Tongue: Hindi

Religion: Hindu

Locality: Urban

Type of family: Nuclear

Number of members in family: 3

Sibling: Single child

Cardinal position of child: Single child

Pregnancy: Wanted, and no infection to mother during pregnancy.

NATAL HISTORY:

Birth place: Hospital

Delivery: Full term and Ceacerian.

Birth cry: Normal

Birth weight: Normal

Colour at birth: Pink

Proper feeding in neonatal period: Yes

Baby respiration: Normal

Proper immunization of mother: Yes

POST NATAL:
Any infection at birth: No

Head injury: No

Convulsions: No

Jaundice: Mild

Nutritional disorder: Yes

Proper immunization: Yes

Problem noted first: At the age of two months and ten days.

After interviewing the parents of Amaaya using a semi-structured interview schedule, the investigator probed into various developmental aspects of Amaaya, her health issues and major concerns of her parents. The same is covered under four sections;

A) Developmental Aspects
B) Major Health Issues
C) Major Concerns of the Parents
D) Treatment and Therapies

A) Developmental Aspects:

1. Physical Development:

Sensory-Motor Development: Sensory and motor development being a gradual process, helps a child to gain use and coordination of large muscles of the legs, trunk, and arms, and smaller muscles of the hands. A child begins to experience new awareness through sight, touch, taste, smell, and hearing.

i. Sensory Development:

- **Vision:** At 7 to 12 months, a baby's vision is the same as an adult's vision. In case of Amaaya, she pays more attention to light up toys/ things. She tries to make good eye contact and if she is in a good mood she tracks people around in the room.
- **Hearing:** At 1 month of age, babies strongly prefer the sound of the human voice. Hearing is the same as an adult's hearing. Amaaya does give reaction to the voices and noises around her.
- **Touch:** She has a well-developed sense of touch. She prefers soft, gentle touches and cuddles.
- **Smell and Taste:** Not very sure about her ability to smell and taste.

ii. Motor Development:

She is not physically strong. She hasn't gained any skills like: sitting, standing, and walking using her hand. Her muscle tone is very low. She seems to be motivated to be active, but she hasn't achieved a lot in terms of development or muscle control.

2. Cognitive and Language Development:

There is no form of verbal communication between Amaaya and her parents. Sometimes she has reached the babbling stage and mumbles words like 'buabua', 'mamama', 'bababa'; however, due to her seizures they are not consistent as she regresses after them. She does respond to the environment around her, if people are calm, she will also remain cool; however, if he hears loud noises and there's an aggressive atmosphere, she reacts to it. Very rarely, Amaaya has shown a positive reaction to what is asked from her by her parents.

3. Emotional and Social Development:

- **Attachment with a Particular Object/ Toy:** Whenever teeth start coming out, every child will have some trouble and they would want to bite things. However, the problem with Amaaya was that she was teething a lot but didn't accept any teether. But when a new toy was given to her, that could be wrapped around her wrist she enjoyed it a lot and used it as a teether. This toy keeps her calm and contented. She would never reach out for a toy; at the same time, she would not hold anything in her hand. That was the reason she did not pick up various teethers and, didn't take them into her mouth. Since this teether is wrapped around her wrist, she doesn't have to grip it and instead has the control.
- **Reaction to Strangers:** She doesn't recognize people, even her parents. She does get along well with caring people and only responds to the emotions. She responds to the person's body language and gestures.
- **Social Behaviour:** Before COVID she used to regularly go out in public places. However, during COVID she has mostly been at home but still enjoys public placed and socialises limitedly. She likes the outdoors more. She is comfortable in crowded places, noisy places and happy places. When there's more life Amaaya feels more comfortable. It all depends on her condition, if she's not feeling good that day, physically or mentally because of her seizure or other issues she might not feel good out as well. When her health is better, her physique and controls are better, she starts noticing kids; which it is a sign that Amaaya is doing better. Unfortunately once the seizures are back, she regresses badly. She has not been noticing kids around these days and even if she does, it is quite mild.

B) Major Health Issues:

Onset of Seizures: When Amaaya was two months and ten days old, her parents first saw her having Tonic-Clonic Seizure. And then, later that week it kept increasing. On the third or fourth day she was admitted as it was getting concerning. The frequency was increasing from once a day to three or four times a day. Duration of her seizures was also increasing from two minutes to ten minutes.

Types of Seizures: Amaaya has a variety of seizures. She has a mixed seizure spectrum. Her Tonic-Clonic Seizures are mostly in control. However, she has had troubles with other seizures, like Tonic with cluster of spasms which may go on for 20 minutes. Depending on her seizure type, her parents have a different attitude. She might have a very quick jerk-like seizure (Drop Seizure) which affects her system. In such situations, her parents cannot do anything as it is like a quick flash and resumes her activities immediately afterwards. She doesn't show any signs of irritation after such seizures. The main concern with Amaaya is Tonic Seizures followed by spasms. Tonic are the ones which really tire her. She has a strong seizure for a few seconds up to a minute during which she holds her breath. Her limbs stiffen contracting her stomach muscles. If her stomach is full, she will vomit. She might also have Absence Seizures and stare at one place; looking left or right. Sometimes, she has seizures in her sleep called Myoclonic Seizures which is a quick jerk-like action in her sleep. These seizures are considered to be rather mild. As the seizures get worse, she also starts having all of them together in a day. That is something which requires professional help.

For her Tonic-Clonic Seizures there are plans for arranging a rescue medication, as for her Tonic spasms there is a planned rescue; however, it is not used often because it is in the form of a tablet and despite it being a disintegrating tablet, her parents fear that she might choke on it. In order to solve this problem, they were advised to keep the tablet under her tongue.

Conditions that make the seizures worse: Her seizures are somewhat in control with the medications. If she doesn't take her medication on time or properly i.e., the right dose is not in her system, she has more seizures. There are other things also which affect her seizure life, for example: food, overexertion and heat. She is content in a cold environment.

C) Parent's Major concerns about Amaaya:

Daily Routine: Amaaya couldn't ever have a proper sleep and wake up routine or feeding routine; however, currently she is a lot better than before. These days Amaaya wakes up in the morning between 6-10 A.M. and takes her medication although, she may or may not take food. She spends a good amount of time in her playpen where she is by herself, either sleeping or doing her activities, which would be just moving around or leaping. She doesn't crawl yet. She can come to a sitting position from a lying position but she cannot sit steady for a long time. She jumps and leaps frequently. Other than that, recently her parents are trying to keep her in a stander for two hours a day. She spends some time in her corner chair, if not that, then a wheelchair. On some days she goes for her therapies. Every two hours, her mother tries to check whether she is accepting food or not. At night she goes to bed. She can nap any time between 8 P.M. to 12 or 1 A.M. She doesn't go to sleep for 10 long hours, despite that her situation has improved a lot as compared to her earlier behaviour.

Difficulty in adjusting to new Routine: There is no set routine for Amaaya. A basic routine that she could follow is of waking up at a certain time and then taking her medication, and having a proper breakfast, lunch and dinner. In addition to that some therapy sessions at home and clinic visits. Her routine is dynamic and depends on health.

- **Feeding and Sleeping Issues:** Her diet is not a normal diet of a 5-year-old. Her meal is carefully planned according to doctor's prescription. These days she is mostly consuming vegetables with some plant-based milk like coconut milk and almond milk occasionally. Good oils like olive oil, coconut oil, and some selected virgin oils etc. are also a part of her diet. Processed foods and dairy are strictly avoided.

Amaaya has a major feeding issue because of her uncontrolled seizures. During her seizure-free period her appetite returns although, she eats a little. However, when they return Amaaya stops eating. She loses her strength and skills and would spend most of her time sleeping.

Amaaya's sleep cycle has also been a matter of great concern for the last few years, especially one and half years ago. Earlier she had seizures only during the day, but a year and half ago she has had them both during the day and night, especially the latter. Her eating and sleeping problems are far more urgent which even surpass her issues with seizures.

- **Random cries and screams:** Amaaya has had episodes where she keeps crying and screaming for long hours. Most of the times she has been inconsolable. However, ever since her seizures are somewhat under control, these activities are not seen as often or aggressively as before. She had a long history of crying for days on end. The longest period was last year in 2020 when she cried continuously for two days; starting Friday evening and only stopping on Sunday evening. This was highly concerning as she was suffering from seizures during that time which were not visible, one of them being Drop Seizures which made it had for her parents to discern whether she had seizures or not.

D) Treatments and Therapies:

She is taking medications as per the doctor's prescriptions. Some days she goes for her therapies, as she is receiving Physical Therapy, Speech Therapy and Occupational Therapy.

CONCLUSION:

CDD being a gene linked disorder poses greater level of health problems to the children suffering with it. Patients living with CDD show a significant neurodevelopmental delay, including severe hypotonia, motor and visual impairment, and little to no communication skills. It is not very easy to take care of a child with CDD. It is suggested that awareness programs should be organized at schools, colleges and at both institutional and local levels to have knowledge and understanding of gene linked diseases or disorders. Further, specialized help and information centres should be opened so that the parents and care takers of children suffering with CDD can have access to it at all times. Moreover, an early diagnosis and early intervention may prove to be helpful in improving the patient's health.

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